REMARKS

Claim 1 was amended by including a feature of Claims 3, 7 and 10.

With respect of Rule 116, entry of the claim amendment is respectfully requested, since the amendment involves a feature that was included in the claims prior to the final rejection.

Claims 1 to 3, 5 to 9 and 12 were rejected under 35 USC 102 as being anticipated by SHIMIZU et al., Journal of Biochemistry, August 2002, 74(8), 4P-459 for the reasons beginning at the middle of page 5 and continuing to the middle of page 6 of the Office Action.

On June 29, 2005, applicants filed a DECLARATION THAT THE INVENTORS NAMED IN THIS APPLICATION ARE THE ONLY PERSONS WHO CONCEIVED AND INVENTED THE SUBJECT MATTER OF THIS APPLICATION WHICH IS DISCLOSED IN A PUBLICATION, executed by the inventors on June 17, 2005.

Paragraph nos. 5 and 6 on page 3 of the aforesaid June 17, 2005 DECLARATION state as follows:

> "5. The non-inventors, who are authors of the aforesaid application (namely authors Ritsuko NARASAKI, Harushige KURIBAYASHI and Tsutomu SATO, only carried out experiments and are not inventors of the above-identified application.
>
> 6. We, Keiji HASUMI and Kosuke SHIMIZU are the only inventors of the above-identified application and, by signing below, we hereby declare that the disclosure in the aforesaid publication was conceived and invented only by us and that the inventorship of the above-identified application is correct in that the publication discloses subject matter derived from us, rather than invented by the authors of the publication that are not inventors, notwithstanding the authorship of the publication."

In view of the above, withdrawal of the 35 USC 102 rejection based on SHIMIZU et al. is respectfully requested.

Claims 1 to 9 and 12 to 14 were rejected under 35 USC 102 as being anticipated by HASUMI et al., "A New Microbiological Enzyme Which Catalyzes Angiostatin Conversion of Plasminogen," Mishima Kaiun Memorial Foundation, Research Report, No. 39, pp. 60-64 for the reasons set forth on page 6 of the Office Action.

The HASUMI publication was cited on a Form PTO/SB/08A attached to applicants' Information Disclosure Statement filed

June 29, 2005.

Submitted comitantly herewith is a DECLARATION UNDER 37 CFR 1.132 (MPEP 715.01(c)) of the joint inventors (Keiji HASUMI and Kosuke SHIMIZU) dated July 26, 2008.

Paragraph no. 3 of said DECLARATION UNDER 37 CFR 1.132 (MPEP 715.01(c)) clarifies that the publication date of HASUMI et al. is December 1, 2002, not "2001" as indicated in the Form PTO/SB/08B dated June 29, 2005. Thus HASUMI et al. is not a reference under 35 USC 102(b).

In paragraph No. 3 of said DECLARATION UNDER 37 CFR 1.132 (MPEP 715.01(c)), the inventors declare that the HASUMI et al. publication is a publication on behalf of the inventors of their joint invention and that the disclosure in the HASUMI et al. publication describes the inventors own work.

In view of the above, withdrawal of the 35 USC 102 rejection based on HASUMI et al. is respectfully requested.

In view of the above, the Examiner is respectfully requested to change the date of the HASUMI et al. publication on the aforesaid Form PTO/SB/08B filed June 29, 2005 to read as follows:

"December 1, 2002."

When the 35 USC 102 rejections based on SHIMIZU et al. and HASUMI et al. are withdrawn, there will be no prior art rejections of claims 4, 13 and 14.

Claims 1 to 3, 5 to 9 and 12 were rejected under 35 USC 102 as being anticipated by McCLUNG et al., Journal of Biomedical Materials Research, (2000), 49(3), pp. 409-414 or RÖMISCH (USP 6,528,299) or FISCHER (USP 6,228,613) for the reasons set forth on pages 4 and 5 of the Office Action.

Claim 1 was amended hereinabove to define the enzyme as bacillolysin MA. It is respectfully submitted that none of the references teach or suggest bacillolysin MA.

In the affinity trap reactor of applicants' present claim 1 comprising a support, an enzyme which is bacillolysin MA and a molecule that specifically binds with a substrate of said enzyme, both the enzyme and the molecule that specifically binds with a substrate of the enzyme, are each bound and immobilized to the support. By using the affinity trap reactor of applicants' present claims, a reaction between an enzyme bound to the

support, and a substrate, can proceed efficiently and rapidly without being affected by spatial restrictions (see page 2, lines 2 to 34 of the present specification).

McCLUNG et al. disclose a blood-contacting surface consisting of a polyurethane to which a coating reagent (polyacrylamide with lysine and benzophenone moieties) is attached, and the surface specifically binds to plasminogen via the lysine moieties (see the Abstract of McCLUNG et al.). Further, it is also suggested that tissue-type plasminogen activator ("t-PA"), an enzyme, binds to the surface lysine moieties via the lysine binding site of kringle 2 of t-PA (see the Conclusions of McCLUNG et al.). Thus, it is definite that t-PA does not directly bind to the surface, but binds to the lysine moieties. Accordingly, the affinity trap reactor of applicants' present claims is substantially different from the surface of McCLUNG et al. in that in applicants' present claims, both an enzyme and a molecule that specifically binds with a substrate of the enzyme are each bound with the support. Thus, applicants' present claims are not anticipated by McCLUNG et al.

RÖMISCH et al. teach merely an affinity chromatography in which heparin is immobilized on a matrix, preferably by using a spacer, lysine, and this is used for selectively binding and then eluting a protease for activating the blood clotting factor VII.

The affinity chromatography in RÖMISCH et al. is quite different from the affinity trap reactor of applicants' present claims in that the chromatography in RÖMISCH et al. does not have both an enzyme and a molecule that specifically binds with a substrate of the enzyme directly binding to the matrix, as the component of such a chromatographic system. Further, the enzyme which binds to the support of the affinity trap reactor of applicants' present claims acts on a substrate, whereas the affinity chromatography in RÖMISCH et al. is used merely to selectively bind and elute a protease, and does not act on the enzyme's substrate. The affinity trap reactor of applicants' present claims is therefore substantially different from the affinity chromatography in RÖMISCH et al. Accordingly, applicants' present claims are not anticipated by RÖMISCH et al.

FISCHER et al. teach merely a heparin affinity chromatography for collecting stable factor VII/vWF-complex, and it is set forth in Example 7 of FISCHER et al. that a plasma